CANCER FACTS
National Cancer Institute • National Institutes of Health

Selenium Supplements Lower Incidence of Lung, Colorectal, and Prostate Cancers

A 10-year cancer prevention trial suggests that dietary supplements of the trace element selenium may significantly lower the incidence of lung, colorectal, and prostate cancers in people with a history of skin cancer. The supplements did not, however, affect the incidence of basal or squamous cell cancers of the skin, the original hypothesis of the study. The results were published in the December 25, 1996, issue of the *Journal of the American Medical Association* (JAMA).*

The study began in l983 and included a total of 1,312 skin cancer patients with a mean age of 63 seen at 7 dermatology clinics in the eastern United States. At that time, the primary purpose of the study was to see if dietary supplements of selenium could lower the incidence of basal cell or squamous cell skin cancers. In 1990, secondary end points, including incidence of three commonly occurring cancers—lung, colorectal, and prostate, were added.

"The results of this study are exciting because they show the cancer prevention potential of a nutritional supplement to a normal diet," said Larry C. Clark, Ph.D., MPH, associate professor of epidemiology at the Arizona Cancer Center in Tucson, Arizona, and principal

* The study is titled: "Effects of Selenium Supplementation for Cancer Prevention in Patients with Carcinoma of the Skin." The authors are Larry C. Clark, Gerald. F Combs Jr., Bruce W. Turnbull, Elizabeth H. Slate, Daniel K. Chalker, James Chow, Loretta S. Davis, Renee A. Glover, Gloria F. Graharn, Earl G. Gross, Arnon Krongrad, Jack Lesher, H. Kim Park, Beverly B. Sanders Jr., Cameron L. Smith, J. Richard Taylor.

investigator of the study. "The study needs to be repeated in other populations before a public health recommendation can be made for selenium supplementation."

Participants in the randomized, double-blinded study (neither patients nor doctors knew who was receiving the intervention) took either a tablet containing 200 micrograms (ug) of selenium as brewer's yeast or a placebo daily for 4.5 years and were followed for an additional 6.4 years. Three-quarters of the participants were men. The trial ended in January 1996, 2 years before the planned end of the trial.

American diets generally include enough grain, meat, and fish, the primary sources of selenium, to meet the recommended dietary allowance (RDA), 70 ug per day for men and 55 ug per day for women. (Although the Environmental Protection Agency established a reference dose of 350 ug per day as a measure of the maximum safe intake, the human toxicity levels for selenium have not been definitely established.)

The study population, however, was from a region of the eastern United States with relatively low selenium levels in soils and crops. Before treatment, participants had a mean plasma selenium concentration in the lower range of the U.S. levels. The supplements increased the plasma concentration by 67 percent and the average daily intake by 3-fold.

The results of the study showed that total cancer incidence was significantly lower in the selenium group than in the placebo group (77 cases versus 119), as was the incidence of some specific cancers: the selenium group had fewer lung cancers (17 versus 31), fewer colorectal cancers (8 versus 19), and fewer prostate cancers (13 versus 35). These differences were statistically significant. The number of cases at other sites was insufficient for a valid analysis.

The results also showed that overall mortality was 17 percent less in the selenium versus the control group (108 versus 129) with this difference largely due to a 50 percent reduction in cancer deaths (29 versus 57). Lung cancer deaths were lower in the selenium treatment group than in the placebo group (12 versus 26). The number of deaths for other cancers was insufficient for meaningful statistical analysis. There was no significant difference between the two groups for other causes of death.

Peter Greenwald, M.D., director of the National Cancer Institute's Division of Cancer Prevention and Control, commented, "These results are interesting for several reasons. First, there was no detectable increase in adverse effects from the supplementation, which is very important to know for future trials. Secondly, beneficial effects were seen for three major cancers.

"Having said all that," he added, "we need to be cautious." Dr. Greenwald noted that the study population was relatively small and consisted of people who live in low-selenium regions and are at high risk for nonmelanoma skin cancer. The lower cancer rates were found for cancers that were secondary, not primary study endpoints. The work, he believes, needs to be confirmed in a larger population more representative of the entire United States.

Selenium soil levels were first associated inversely with cancer mortality in the late 1960s. Similar results were found in prospective studies that measured selenium status by several methods: soil, blood, nails, and hair. Some studies have also found inverse associations with the incidence of cancers of the lung, colon, bladder, rectum, breast, pancreas, and ovary. However, several other studies have shown no association between selenium status and cancer, and a few have shown a direct association (i.e., increased cancer risk associated with increased selenium status).

In animals, selenium administration has been shown to have antitumor activity, but at levels several times greater than the nutritional needs. Likewise, in tissue culture experiments, supplementation of cultured tumor cells with selenium at much higher doses than the cells normally require has been shown to inhibit tumor growth and stimulate apoptosis (programmed cell death).

Three human intervention studies with selenium have had various outcomes. The low soil selenium content in Finland led the Finnish government to begin adding selenium to fertilizers in l984 with an eye towards reducing the risk of cancer and cardiovascular disease. No significant effects on cancer incidence have been seen to date in the Finnish population of four million.

Two additional human intervention trials took place in Linxian, China, from l985 to 1991. In one trial, a daily supplement containing 50 ug of selenium plus three other minerals and vitamins had no effect on the high incidence of esophageal cancer or total cancer incidence or mortality. The second and larger trial showed a significant reduction in stomach cancer incidence (16 percent) and stomach cancer mortality (21 percent) using a daily mixture of antioxidants, one component of which was selenium.

The study described in the 1996 JAMA article is the first double-blinded cancer prevention trial to test whether a nutritional supplement of selenium alone can reduce cancer risk. Participating dermatology clinics were located in Augusta, Georgia; Macon, Georgia; Columbia, South Carolina; Miami, Florida; Wilson, North Carolina; Greenville, North Carolina; and Newington, Connecticut.

Dr. Greenwald commented on the possibility of future prevention trials. "This study highlights the value of clinical trials in cancer prevention. The interesting observation of a possible benefit of selenium needs to be assessed in a larger, more definitive trial."

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1–800–4–CANCER (1–800–422–6237)
TTY (for deaf and hard of hearing callers): 1–800–332–8615

NCI Online

Internet

Use http://www.cancer.gov to reach NCI's Web site.

CancerMail Service

To obtain a contents list, send e-mail to cancermail@icicc.nci.nih.gov with the word "help" in the body of the message.

CancerFax® fax on demand service

Dial 301–402–5874 and listen to recorded instructions.

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